

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

Claims 1-47 (Canceled)

Claim 48. (Previously Presented) A method of staining target chromosomal material comprising:

- (a) providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb, which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal material for which detection is desired, and providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid; and
- (b) employing said labeled nucleic acid probe, blocking nucleic acid, and chromosomal DNA in *in situ* hybridization so that labeled repetitive segments, if present, are substantially blocked from binding to the chromosomal DNA, while hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, wherein blocking of the labeled repetitive segments is sufficient to permit detection of hybridized labeled nucleic acid containing unique segments, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the *in situ* hybridization.

Claim 49. (Previously Presented) The method of claim 48, wherein the chromosomal DNA is present in a morphologically identifiable chromosome.

Claim 50 (Canceled)

Claim 51. (Previously Presented) The method of claim 48, wherein the chromosomal material is from a fetal cell.

Claim 52. (Previously Presented) The method of claim 49, further comprising the step of separating the fetal cell from maternal blood.

Claim 53. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid probe comprises heterogeneous mixtures of labeled nucleic acid fragments, wherein the nucleic acid fragments are substantially complementary to sites on the targeted chromosomal material and are substantially free of nucleic acid sequences having a hybridization capacity to sites on chromosomal material that is not targeted.

Claim 54. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing chromosomes.

Claim 55. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing portions of a chromosome.

Claim 56. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of chromosomal rearrangement.

Claim 57. (Previously Presented) The method of claim 56, wherein the chromosomal rearrangement is an inversion.

Claim 58. (Previously Presented) The method of claim 56, wherein the chromosomal rearrangement is an insertion.

Claim 59. (Previously Presented) The method of claim 56, wherein the chromosomal rearrangement is a translocation.

Claim 60. (Previously Presented) The method of claim 56, wherein the chromosomal rearrangement is an amplification.

Claim 61. (Previously Presented) The method of claim 56, wherein the chromosomal rearrangement is a deletion.

Claim 62. (Previously Presented) The method of claim 48, wherein the target chromosomal material is present in an interphase cell nucleus.

Claim 63. (Previously Presented) The method of claim 62, wherein the labeled nucleic acid has a complexity of between about 40 kb and 100 kb.

Claim 64. (Previously Presented) The method of claim 62, wherein the labeled nucleic acid has a complexity between about 50 kb and 400 kb.

Claim 65. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to the total genomic complement of chromosomes.

Claim 66. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a single chromosome.

Claim 67. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a subset of chromosomes.

Claim 68. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a subregion of a single chromosome.

Claim 69. (Previously Presented) The method of claim 48, wherein the labeled nucleic acid is designed to allow detection of cancer.

Claim 70 (Canceled)

Claim 71. (Previously Presented) The method of claim 48, further comprising removing from the labeled nucleic acid fragments which are substantially complementary to repetitive segments within the target chromosomal material.

Claim 72. (Previously Presented) A method of staining target interphase chromosomal DNA comprising:

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal DNA for which detection is desired, wherein the nucleic acid probe is substantially free of repetitive segments which are complementary to repetitive segments in the target interphase chromosomal material; and

(b) employing said labeled nucleic acid probe and chromosomal DNA in *in situ* hybridization so that hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, and hybridized labeled nucleic acid containing unique segments are detected, and wherein the interphase chromosomal DNA is present in a morphologically identifiable cell nucleus during the *in situ* hybridization.

73. (Currently amended) ~~The A method of claim 72, of staining target interphase chromosomal DNA comprising:~~

providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal DNA for which detection is desired, wherein the nucleic acid probe is substantially free of repetitive segments which are complementary to repetitive segments in the target interphase chromosomal material; further comprising

providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid probe and employing said labeled nucleic acid probe, blocking nucleic acid, and chromosomal DNA in *in situ* hybridization so that hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, labeled repetitive segments, if present, are substantially blocked from binding to the chromosomal DNA, and hybridized labeled nucleic acid containing unique segments are detected, and wherein the interphase chromosomal DNA is present in a morphologically identifiable cell nucleus during the *in situ* hybridization.

Claims 74-75 (Canceled)

Claim 76. (Previously Presented) The method of claim 72, wherein the chromosomal material is from a fetal cell.

Claim 77. (Previously Presented) The method of claim 76, further comprising the step of separating the fetal cell from maternal blood.

Claim 78. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid probe comprises heterogeneous mixtures of labeled nucleic acid fragments, wherein the nucleic acid fragments are substantially complementary to sites on the targeted chromosomal material and are substantially free of nucleic acid sequences having a hybridization capacity to sites on chromosomal material that is not targeted.

Claim 79. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing chromosomes.

Claim 80. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing portions of a chromosome.

Claim 81. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of chromosomal rearrangement.

Claim 82. (Previously Presented) The method of claim 81, wherein the chromosomal rearrangement is an inversion.

Claim 83. (Previously Presented) The method of claim 81, wherein the chromosomal rearrangement is an insertion.

Claim 84. (Previously Presented) The method of claim 81, wherein the chromosomal rearrangement is a translocation.

Claim 85. (Previously Presented) The method of claim 81, wherein the chromosomal rearrangement is an amplification.

Claim 86. (Previously Presented) The method of claim 81, wherein the chromosomal rearrangement is a deletion.

Claim 87 (Canceled)

Claim 88. (Previously Presented) The method of claim 87, wherein the labeled nucleic acid has a complexity of between about 40 kb and 100 kb.

Claim 89. (Previously Presented) The method of claim 87, wherein the labeled nucleic acid has a complexity between about 50 kb and 100 kb.

Claim 90. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to the total genomic complement of chromosomes.

Claim 91. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to a single chromosome.

Claim 92. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to a subregion of a single chromosome.

Claim 93. (Previously Presented) The method of claim 72, wherein the labeled nucleic acid is designed to allow detection of cancer.

Claim 94 (Canceled)

Claim 95. (Previously Presented) The method of claim 72, wherein the targeted chromosomal material is a genetic rearrangement associated with chromosome 21 in humans.

Claim 96. (Previously Presented) The method of claim 72, wherein fragments substantially complementary to repetitive segments in the target interphase chromosomal material are removed from the labeled nucleic acid probe.

Claim 97. (Previously Presented) The method of claim 72, wherein the complexity of the labeled nucleic acid probe is greater than about 200 kb.

Claim 98. (Previously Presented) A method of staining target chromosomal material comprising:

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 50 kb, which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal material for which

detection is desired, and providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid; and

(b) employing said labeled nucleic acid probe, blocking nucleic acid, and chromosomal DNA in *in situ* hybridization so that labeled repetitive segments, if present, are substantially blocked from binding to the chromosomal DNA, while hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, wherein blocking of the labeled repetitive segments is sufficient to permit detection of hybridized labeled nucleic acid containing unique segments, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the *in situ* hybridization.

Claim 99. (Previously Presented) The method of claim 98, wherein the target chromosomal material is present in an interphase cell nucleus.

Claim 100. (Previously Presented) The method of claim 99, wherein the labeled nucleic acid has a complexity of between about 50 kb and 400 kb.

Claim 101. (Previously Presented) The method of claim 100, wherein the labeled nucleic acid has a complexity between about 50 kb and 100 kb.

Claim 102. (Previously Presented) A method of staining target interphase chromosomal DNA comprising:

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 50 kb which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal DNA for which detection is desired, wherein the nucleic acid probe is substantially free of repetitive

segments which are complementary to repetitive segments in the target interphase chromosomal material; and

(b) employing said labeled nucleic acid probe and chromosomal DNA in *in situ* hybridization so that hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, and hybridized labeled nucleic acid containing unique segments are detected, and wherein the interphase chromosomal DNA is present in a morphologically identifiable cell nucleus during the *in situ* hybridization.

Claim 103. (Previously Presented) The method of claim 102, wherein the labeled nucleic acid has a complexity of between about 50 kb and 400 kb.

Claim 104. (Previously Presented) The method of claim 103, wherein the labeled nucleic acid has a complexity between about 50 kb and 100 kb.